Remarks

Claims 35-54 and 59-79 are elected for examination in this application. Withdrawn claims have been cancelled as well as claims 64-84. Applicants intend to file one or more continuation applications directed to cancelled claims.

An Information Disclosure Statement containing previously submitted citations has been resubmitted on January 13, 2008, so that paper copies can be supplied. Consideration of each reference and an acknowledgement of the consideration is respectfully requested.

The Rejection of Claims 70-72 Under 35 U.S.C. § 102 (b)

Claims 70-72 were rejected as anticipated by Ghadessy (Proc. Natl. Acad. Sci. U.S.A., 2001). These claims have been cancelled, rendering this rejection moot.

The Rejection of Claims 35-38, 40-41, 44-52, 54, 59-61, and 63-79 Under 35 U.S.C. § 102 (e)

Claims 35-38, 40-41, 44-52, 54, 59-61, and 63-79 stand rejected as anticipated by Leamon (U.S. 7323305). Leamon was filed on 28 January 2004[1], after the effective filing date of the subject application of July 5, 2003. Leamon is prior art under § 102(e) to the subject application only if its priority applications describe Dressman's invention. Leamon claims the benefit of seven provisional applications. Two of the seven are indicated by the U.S. Patent and Trademark Office to be relevant to the subject matter claimed in the subject Dressman application. The other five disclose different subject matter. The two provisional applications

[1] A certificate of correction has not yet been issued to acknowledge this as the filing date. The face of the patent currently lists September 22, 2004 as the filing date. Without the corrected filing date, Leamon's priority claims are ineffective for failing to comply with 35 U.S.C. § 119(e).

identified by the U.S. Patent and Trademark Office are:

- 60/465071 filed April 23, 2003; and
- 60/476504 filed June 6, 2003.

Leamon is not an effective reference against the subject claims as of April 23, 2003. Leamon's provisional application 60/465071 does not describe or enable the subject matter of the rejected claims.

Leamon's provisional application 60/476504, *i.e.,* June 6, 2003 is not effective prior art because the current applicants invented before that date. Applicants provide a Declaration Under Rule 131 demonstrating that the applicants invented the subject matter of the claims prior to June 6, 2003. A Rule 131 declaration showing an earlier date of invention is appropriate because Leamon does not claim the same invention as the subject claims. In view of these facts, Leamon U.S. 7323305 does not constitute effective prior art with regard to the subject application's claims.

1. Leamon 60/465071 filed April 23, 2003 does not provide an effective filing date.

a. Leamon 60/465071 filed April 23, 2003 does not teach the subject invention.

Leamon's priority application 60/465071 filed April 23, 2003 does not describe the subject matter of the rejected claims. Therefore, even if Leamon's **later** applications described the subject application, they cannot be applied with an effective date of April 23, 2003 with regard to the subject application.

Most of Leamon's 60/465071 filed April 23, 2003 disclosure is directed to totally distinct subject matter. Only a very brief portion is potentially relevant to the currently claimed subject matter. The possibly relevant disclosure appears in two paragraphs, beginning with the paragraph spanning pages 46 and 47. It teaches:

A second approach to amplifying and capturing both strands will be to amplify the fragment library offline in a single tube using oil and surfactant-based emulsions to encapsulate the capture beads, template and PCR reaction mix. This approach will maintain the clonality of the amplification, provide

a single-tube format for second strand removal, sequencing primer annealing and the addition of signal-producing enzymes. The average size of the emulsion capsules must be optimized to maximize the number of single beads containing single strands of DNA, that can be incorporated within a single emulsion volume. An adequate volume-to-bead ratio must be maintained in order to insure a maximum number single bead capsules. Consequently we anticipate that the emulsion volumes must continue to increase to allow for capture of increasingly larger numbers of fragments from larger genomes. The single, large volume of the emulsion PCR mix can be aliquoted into standard PCR tubes and all aliquots run simultaneously in a standard thermalcycler. Bead-to-emulsion volume ratios must be adequate to accommodate a balance between total volume and absolute bead numbers. Smaller genomes can be amplified in single PCR tubes allowing for many whole genome libraries to be amplified at the same time. We will attempt to limit the total volume of emulsion without expanding the amplification effort beyond a full 96-well thermalcycler.

Sequencing.

Each bead is covalently loaded with large numbers of two oligonucleotides complementary to the 3' ends of our two universal linker sequences found on each strand of the amplified product. We will specifically capture the single stranded forms of the complementary strands of an amplified DNA fragment by using these two oligonucleotides. These oligonucleotides are each targeting the 3' end of their respective stands. Both capture oligonucleotides are conjugated to the solid phase capture bead resulting in the simultaneous capture of the many copies of each strand on the same single bead in a single well. In turn, we must then anneal sequencing primers to these fragments and perform our initial sequencing reaction to obtain 50 to 100 bases of sequence from one strand. Both sequencing primers will be annealed simultaneously to their respective single stranded templates. The two primers will differ in their construction in that the complementary strand primer will contain a 3' PO4 or comparable moiety to block the polymerase from binding and extending the primer during the first round of sequencing. As the first strand sequencing reaches maximum read length, we will terminate the reaction and render the first template inactive. The system will be washed to remove nucleotides and subsequently treated with an appropriate phosphatase or chemistry to remove the 3' blocker from the second sequencing primer. This will activate the primer as a substrate for the DNA polymerase and another round of sequencing. The remainder of the sequencing run will be performed as for the first strand. It appears that the second-strand sequencing portion of our proposed process may not be as robust as the first strand despite using the identical method. One cause that we have identified in our current system appears to be due to deoxynucleotide triphophates (dNTP's) being left behind in the wells after our washes. These "left behind" dNTP's become available for subsequent rounds of synthesis and create false positive signals. We will test the use of nucleosidases, longer or faster washes or different wash components such as detergents and/or hydrophilic polymers in our wash buffers. A secondary cause of poor second-strand sequencing could be the incomplete removal of PO4 or blocking molecule for the 3' end of the second sequencing primer, reducing sequence initiation. We will test a collection of phosphatases for efficiency of removing the 3' phosphate. We will also try other blocking molecules such a ribonucleotide triphosphates (rNTP) or alpha S-dNTP.

Leamon '071 does not teach critical aspects of the claimed invention. Leamon '071 does not teach:

- wherein the reagent beads are bound to a plurality of molecules of a primer for amplifying the analyte DNA molecules, whereby product beads are formed which are bound to a plurality of copies of one species of analyte DNA molecule (claims 35 and 59);
- separating the product beads from analyte DNA molecules which are not bound to product beads (claims 35 and 59);
- isolating product beads which are bound to a plurality of copies of a first species of analyte DNA molecule from product beads which are bound to a plurality of copies of a second species of analyte DNA molecule (claims 36 and 59).

Rather than teaching that the beads comprise primers and that the step of amplifying results in the amplified products covalently attached to the beads as a result of amplification, Leamon '071 teaches amplification in solution using primers in solution, followed by a step of binding the amplification products to the beads. "We will specifically capture the single stranded forms of the complementary strands of an amplified DNA fragment by using these two oligonucleotides. These oligonucleotides are each targeting the 3' end of their respective strands. Both capture oligonucleotides are conjugated to the solid phase capture bead resulting in the simultaneous capture of the many copies of each strand on the same single bead in a single well." Page 47, lines 15-18; emphasis added. Leamon does not teach the element of amplifying onto the bead, but rather amplification in solution followed by simultaneous capture on a bead.

Perhaps as a consequence of not teaching amplifying onto the beads, Leamon '071 does not teach or mention the need to separate product beads (with bound analyte DNA molecules) from analyte DNA molecules which are not bound. Regardless of the reason, Leamon '071 does not teach this aspect of the claimed invention.

Leamon '071 does not teach the aspect of isolating product beads which are bound to a first analyte from those bound to a second analyte. Such a teaching is notably absent in Leamon '071.

For these reasons, it is respectfully submitted that Leamon '071 does not describe the subject matter of the rejected claims. Therefore, the Leamon patent U.S. 7323305 is not effective prior art to the subject claims as of April 23, 2003.

b. Leamon 60/465071 filed April 23, 2003 does not enable the subject invention.

Leamon '071 also does not enable the subject invention. Leamon '071 is decidedly silent on how even its method can be practiced; it certainly does not teach how the method of the subject application can be practiced. Leamon '071 raises a number of issues of operation that have apparently not been solved as of the date of April 23, 2003. Leamon '071 raises the issue of the proper size of the emulsion capsules and the appropriate volume-to-bead ratio. Although these are couched in the language of optimization, there are absolutely no guidelines provided to enable one of skill in the art to practice the invention, even without optimization. Thus it is respectfully submitted that Leamon '071 does not enable the subject matter of the claimed invention. For this reason as well, the Leamon patent U.S. 7323305 is not effective prior art to the subject claims as of April 23, 2003.

2. Leamon 60/476504 filed June 6, 2003 was filed after applicants made the subject invention.

a. Rule 131 declaration demonstrates an invention date prior to June 6, 2003.

Applicants concurrently submit a Rule 131 Declaration that demonstrates that applicants made the invention in the U.S. prior to the date of the latter of the two possibly relevant provisional applications of Leamon, *i.e.*, 60/476504. Rule 131 states that "[p]rior invention may not be established under this section if ....(1) The rejection is based upon a U.S. patent or U.S. patent application publication of a pending or patented application to another or others which claims the same patentable invention as defined in §41.203(a) of this title, in which case an applicant may suggest an interference pursuant to §41.202(a) of this title...."

The Rule 131 Declaration shows that each of the limitations of independent claims 35 and 59 was actually performed in the U.S. prior to June 6, 2003, and reported in the manuscript submitted June 6, 2003.[2]

Claim Element	Claim recitation	Manuscript location	Manuscript teaching
35, preamble	A method for analyzing nucleotide sequence variations, comprising:	Page 8819, last paragraph	We generally used hybridization of fluorescein-conujgated or biotin – conjugated oligonucleotides for discrimination.
35, step 1	forming microemulsions comprising one or more species of analyte DNA molecules;	Page 8817, last paragraph, page 8818 last paragraph, Fig. 2	Step 2: Preparing Microemulsions. Microemulsions for PCR were prepared by slight modifications of described methods (14, 15). The oil phase was composed of 4.5% Span 80 (no. S6760, Sigma), 0.40% Tween 80 (no. S-8074, Sigma), and 0.05% Triton X-100 (no. T9284, Sigma) in mineral oil (no. M-3516, Sigma). The oil phase was freshly prepared each day. The aqueous phase consisted of 67 mM Tris·HCl (pH 8.8), 16.6 mM NH4SO4, 6.7 mM MgCl2, 10 mM 2-mercaptoethanol, 1 mM dATP, 1 mM dCTP, 1 mM dGTP, 1 mM dTTP, 0.05 μM forward primer, 25 μM reverse primer, 45 units of Platinum Taq (no. 10966-034, Invitrogen), various amounts of template DNA (see Results), and ≈108 oligonucleotide-coupled beads in a total volume of 300 μl. The forward primer was an oligonucleotide with a sequence that was identical to the 3′ 20–22 nt of that described in step 1 and was not modified with biotin. Step 2: Preparing Microemulsions. The size of the individual aqueous compartments were 5.4 ± 2.7 μm in diameter (Fig. 2). We estimated that an emulsion comprising 200 μl of aqueous solution and 400 μl of oil would contain ≈3 × 109 compartments with an average

2 Applicants reserve the right to present additional documents and evidence to establish that the were in possession of the invention prior to June 6, 2003.

Claim Element	Claim recitation	Manuscript location	Manuscript teaching
			diameter of 5 μm. Approximately 108 beads were included in each emulsion such that only one in ≈30 compartments contained a bead. The optimal amount of template was experimentally determined to be ≈5 × 108 molecules, so that one in approximately six compartments contained a template molecule. Fig. 2. Photograph of a typical microemulsion. Microemulsions were made as described in Materials and Methods with the exception that the aqueous compartments contained cascade blue-labeled dCTP and the beads were prelabeled by binding to oligonucleotides coupled to R-phycoerythrin (red) or Alexa 488 (green). One microliter of microemulsion was deposited in 1 μlofoil on a microscope slide before photography. Of the seven aqueous compartments visible in this picture, two contain beads. Note the heterogeneous size of the aqueous compartments (beads are 1.05 μm in diameter).
35, step 2	amplifying analyte DNA molecules in the microemulsions in the presence of reagent beads, wherein the reagent beads are bound to a plurality of molecules of a primer for amplifying the analyte DNA molecules,	Page 8818, second full paragraph and page 8819, first full paragraph	Step 3: PCR Cycling. The emulsions were aliquoted into five wells of a 96-well PCR plate, each containing 100 μl. PCR was carried out under the following cycling conditions: 94°C for 2 min, 40 cycles of 94°C for 15 sec, 57°C for 30 sec, and 70°C for 30 sec. The PCR products analyzed in this study ranged from 189 to 239 bp. Step 3: PCR Cycling. PCR priming by oligonucleotides coupled to beads was found to be very inefficient compared with the priming by the same oligonucleotides when free in solution. For this reason, a small amount of nonbiotinylated forward primer identical

Claim Element	Claim recitation	Manuscript location	Manuscript teaching
			in sequence to the biotinylated oligonucleotide coupled to the beads was included in the reactions. This facilitated the first few rounds of amplification of the single template within each aqueous compartment. In the absence of additional primer, no detectable amplification on the beads was generated. Conversely, if too much additional primer was included, no amplification on the beads occurred because of competition with the primers in solution. An excess of the reverse primer was included in the aqueous compartment to maximize the probability that bead-bound oligonucleotides extended by polymerase would serve as templates for further amplification cycles.
35, step 2	whereby product beads are formed which are bound to a plurality of copies of one species of analyte DNA molecule;	Page 8819, last full paragraph and page 8820 fifth full paragraph and Fig. 3.	By measuring the amount of DNA that could be released from the beads after restriction endonuclease digestion, we estimate that >10,000 extended PCR products were present, on average, per bead. Fig. 3 *B–D* show density plots of gated beads generated with various templates. In Fig. 3*B*, a template from an individual homozygous for the *L* allele was included in the emulsion. Two populations of beads were apparent. Ninety-eight percent of the beads contained no PCR product (black), and the remaining 2% fluoresced in the FL1 channel (colored green in Fig. 3). Fig. 3*C* represents the analysis of an individual homozygous for the *S* allele. Two populations of beads were again apparent, but this time the labeled population fluoresced in the FL2 channel (colored red in Fig. 3). Fig. 3*D* presents density plots from the analysis of an individual heterozygous at the *MID42*

Claim Element	Claim recitation	Manuscript location	Manuscript teaching
			locus. Four populations of beads are evident: the black region represents beads without any PCR product; the red region represents beads containing PCR products from the *S* allele; the green region represents beads containing PCR products from the *L* allele; and the blue region represents beads containing PCR products from both alleles. Beads containing PCR products from both alleles were derived from aqueous compartments that contained more than one template molecule. The number of such beads increased in a nonlinear fashion as more template molecules were added. At the extreme, when all aqueous compartments are saturated, virtually all beads will register as blue. Operationally, we found that the bead populations were most distinct when the number of beads containing any PCR product was <10% of the total beads analyzed. Fig. 3. Density plots of flow-cytometric data obtained from BEAMing. The locus queried in this experiment was MID42, and PCR products generated from genomic DNA were used as templates in the microemulsions. (A) Forward scatter (FSC) and side scatter (SSC) of all beads show that ≈80% of the total beads are singlets, with most of the remaining beads aggregated as doublets. The "noise" is instrumental and is observed with blank samples containing no beads. The instrument output was gated such that only singlets were analyzed for fluorescence analysis. The patterns observed from an individual homozygous for the L allele (A), homozygous for the S allele (B), and heterozygous for L and S (D) are shown in B–D, respectively. The regions

Claim Element	Claim recitation	Manuscript location	Manuscript teaching
			containing beads hybridizing to the L and S allele probes are labeled green and red, respectively. The region containing beads that did not hybridize to any probe is black, and the region containing beads that hybridized to both probes is blue. The blue beads arose from aqueous compartments in which both types of template molecules were present. The proportion of singlet beads that hybridized to at least one of the probes was 2.9%, 4.3%, and 20.3% in B–D, respectively. The forward-scatter and side-scatter plots in A represent the same beads analyzed in D. FL1, fluorescent channel 1; FL2, fluorescent channel 2; PE, R-phycoerythrin.
35, step 3	separating the product beads from analyte DNA molecules which are not bound to product beads;	Page 8818, third full paragraph	Step 4: Magnetic Capture of Beads. After PCR cycling, the microemulsion from five wells of a PCR plate were pooled and broken by the addition of 800 μl of NX buffer (100 mM NaCl/1% Triton X-100, 10 mM Tris·HCl, pH 7.5, and 1 mM EDTA) in a 1.5-ml tube (no. 430909, Corning). After vortexing for ≈20 sec, the beads were pelleted by centrifugation in a microcentrifuge at 8,000 rpm (5,000 × g) for 90 sec. The top oil phase and all but ≈300 μl of the aqueous phase were removed from the tube, and 600 μl of NX buffer was added. After vortexing for 20 sec and centrifugation for 90 sec, the top oil phase and all but ≈300 μl of the aqueous phase were removed. The addition of 600 μl of NX buffer, vortexing, and centrifugation were repeated once more, and the top oil portion and all but ≈300 μl of the aqueous phase were removed. The tube then was placed on a magnet (MPC-S, Dynal), and the rest of the supernatant was pipetted off carefully.

Claim Element	Claim recitation	Manuscript location	Manuscript teaching
			The beads were washed an additional three times with 1× PCR buffer by using magnetic separation rather than centrifugation and finally resuspended in 100 μl of 1× PCR buffer.
35, step 4	determining a sequence feature of the one species of analyte DNA molecule which is bound to the product beads.	Figs. 3, 4, 5	Fig. 3. Density plots of flow-cytometric data obtained from BEAMing. The locus queried in this experiment was MID42, and PCR products generated from genomic DNA were used as templates in the microemulsions. (A) Forward scatter (FSC) and side scatter (SSC) of all beads show that ≈80% of the total beads are singlets, with most of the remaining beads aggregated as doublets. The "noise" is instrumental and is observed with blank samples containing no beads. The instrument output was gated such that only singlets were analyzed for fluorescence analysis. The patterns observed from an individual homozygous for the L allele (A), homozygous for the S allele (B), and heterozygous for L and S (D) are shown in B–D, respectively. The regions containing beads hybridizing to the L and S allele probes are labeled green and red, respectively. The region containing beads that did not hybridize to any probe is black, and the region containing beads that hybridized to both probes is blue. The blue beads arose from aqueous compartments in which both types of template molecules were present. The proportion of singlet beads that hybridized to at least one of the probes was 2.9%, 4.3%, and 20.3% in B–D, respectively. The forward-scatter and side-scatter plots in A represent the same beads analyzed in D. FL1, fluorescent channel 1; FL2, fluorescent channel 2; PE, R-phycoerythrin.

Claim Element	Claim recitation	Manuscript location	Manuscript teaching
			Fig. 4. Density plots of BEAMing with genomic DNA or RT-PCR products as templates. The data in A and B were generated by including 10 and 1 μg of human genomic DNA, respectively, in the microemulsions, querying the MID42 locus. The data in C and D were generated by using emulsions that contained ≈50 pg of PCR products synthesized from cDNA of lymphoblastoid cells, querying the calpain-10 locus. The green and red regions correspond to the L and S alleles for MID42 and to the A and G alleles for calpain-10. The number of beads in the outlined regions containing red or green beads is shown in each case. The proportion of singlet beads that hybridized to at least one of the probes was 1.2%, 0.6%, 6.8%, and 4.2% in A–D, respectively. The outlined regions used for counting in A and B were identical, as were those used for C and D. Beads that did not hybridize to any probe were gated out and therefore not evident in the graphs, and the region containing beads that hybridized to both probes is labeled blue. FL1, fluorescent channel 1; FL2, fluorescent channel 2; PE, R-phycoerythrin. Fig. 5. Detection and validation of variants present in a minor fraction of the DNA population. (A) Mixtures of PCR products containing 0–4% L alleles of MID42 were used for BEAMing. Flow cytometry such as that shown in Fig. 3 was used to determine the fraction of singlet beads that were red (y axis). The proportion of singlet beads that hybridized to at least one of the probes varied from 3.2% to 4.3%. (B and C) Beads were sorted with the

Claim Element	Claim recitation	Manuscript location	Manuscript teaching
			FACSVantage SE instrument, and individual red or green beads were used as templates for conventional PCR by using the forward and reverse primers listed in Table 1. Red beads generated only the S allele sequence, whereas green beads generated only the L allele sequence.
59, preamble	A method for isolating nucleotide sequence variants, comprising:	Page 8821, last paragraph spanning to page 8822	The rare beads representing the mutant alleles could not only be quantified but also purified for subsequent analysis. As a demonstration, samples of the beads enumerated in Fig. 5A were assessed by using a flow cytometer equipped with sorting capabilities. Beads were sorted and individual beads were used as templates for conventional PCR by using the same primers used for BEAMing. Because each bead contains thousands of bound template molecules, single beads were expected to generate robust PCR products (23), and this was confirmed experimentally. These PCR products then were subjected to sequencing. As shown in Fig. 5 B and C, green and red beads generated PCR products exclusively of the L and S types, respectively.
59, step 1	forming microemulsions comprising one or more species of analyte DNA molecules;	See claim 35, step 1	See above
59, step 2	amplifying analyte DNA molecules in the microemulsions in the presence of reagent beads, wherein the reagent	See claim 35, step 2	See above

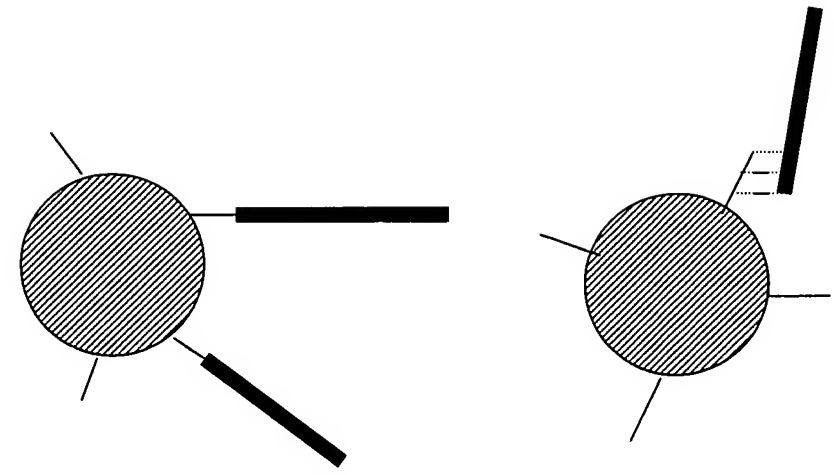
Claim Element	Claim recitation	Manuscript location	Manuscript teaching
	beads are bound to a plurality of molecules of a primer for amplifying the analyte DNA molecules, whereby product beads are formed which are bound to a plurality of copies of one species of analyte DNA molecule;		
59, step 3	separating the product beads from analyte DNA molecules which are not bound to product beads;	See claim 35, step 3	See above
59, step 4	isolating product beads which are bound to a plurality of copies of a first species of analyte DNA molecule from product beads which are bound to a plurality of copies of a second species of analyte DNA molecule.	Page 8818, column 2, first full paragraph; page 8821-8822, spanning paragraph	In some cases, scanning was performed with FACScan or FACSCalibur instruments (BD Biosciences), yielding equivalent results. Sorting was carried out with a FACSVantage SE instrument (BD Biosciences). The flow-cytometry data were analyzed by using cellquest software (BD Biosciences). The rare beads representing the mutant alleles could not only be quantified but also purified for subsequent analysis. As a demonstration, samples of the beads enumerated in Fig. 5A were assessed by using a flow cytometer equipped with sorting capabilities. Beads were sorted and individual beads were used as templates for conventional PCR by using the same primers used for BEAMing. Because each bead contains thousands of bound template molecules, single beads were expected to generate robust PCR

Claim Element	Claim recitation	Manuscript location	Manuscript teaching
			products (23), and this was confirmed experimentally. These PCR products then were subjected to sequencing. As shown in Fig. 5 B and C, green and red beads generated PCR products exclusively of the L and S types, respectively.

Thus, the applicants reduced to practice their invention prior to June 6, 2003. Leamon 60/476504 is not prior art to the invention.

b. Leamon U.S. Patent 7,323,305 does not claim the same invention

Leamon does not claim the same invention as the subject claims. As discussed above, the Leamon provisional application '071 did not teach amplification onto a bead. Similarly, the claims of U.S. Patent 7,323,305 ('305) do not recite amplification onto a bead. Rather the amplification is performed in solution and subsequently bound to the beads ("amplifying...and binding the amplified copies to beads in the microreactors"). The difference between these two methods results in different products. Leamon's product beads are attached to an oligonucleotide which is ***hybridized to a portion of*** a single stranded amplification product. The present invention's product beads are attached to an oligonucleotide which is ***covalently linked to*** an amplification product. In the drawing below, the black bar represents the amplification products, the circles represent beads, and the protrusions from the circles represent oligonucleotides. The amplification products in the Dressman method are covalently linked to the oligonucleotide attached to the bead, whereas in the Leamon method, the amplification product is (non-covalently) hybridized to a complementary oligonucleotide attached to the bead.



Moreover, the sole independent claim of the Leamon '305 patent requires three steps that are not recited in the subject claims. The '305 patent claim 1 requires "fragmenting large template nucleic acid molecules to generate a plurality of fragmented nucleic acid molecules" (step (a)); "delivering the beads to an array of at least 10,000 reaction chambers on a planar surface, wherein a plurality of the reaction chambers comprise no more than a single nucleic acid bound bead" (step (d)); "performing a sequencing reaction simultaneously on a plurality of the reaction chambers" (step (e)).

In addition, independent claims 35 and 59 of the subject application recite a step which is not found in the '305 patent claims: "separating the product beads from analyte DNA molecules which are not bound to product beads."

For all these reasons Leamon '305 does not claim the same invention as the subject application.

3. Summary

Applicants request withdrawal of the rejection of claims 35-38, 40-41, 44-52, 54, 59-61, and 63 as anticipated by Leamon (U.S. 7323305). The remarks detail that the April 23 provisional application ('071) does not describe and enable the subject matter of the claimed invention. The Declaration Under Rule 131 indicates that the Dressman et al. inventors invented prior to the date of the June 6 provisional of Leamon (60/476592). The other priority applications of Leamon are not relevant. Withdrawal of the rejection under § 102(e) is therefore appropriate.

The Rejection of Claims 39, 43, and 62 Under 35 U.S.C. 103(a)

Claims 39, 43, and 62 stand rejected as unpatentable over Leamon U.S. 7323305. As demonstrated above with respect to the independent claims from which claims 39, 43, and 62 depend, Leamon does not constitute effective prior art against the subject application. This is true whether in the context of a Section 102 or 103 rejection. Therefore, for the same reasons as provided above, this rejection should be withdrawn.

The Rejection of Claim 42 Under 35 U.S.C. 103(a)

Claim 42 is separately rejected as unpatentable over Leamon U.S. 7323305 in view of Becker (U.S. 5546792). Leamon has been discussed above. Becker is cited as teaching the breaking of emulsions using detergent. It is respectfully submitted that this rejection should be withdrawn for the same reasons as discussed for prior rejections: Leamon does not constitute effective prior art against the subject application. Withdrawal is respectfully requested.

The Rejection of Claim 53 Under 35 U.S.C. 103(a)

Claim 53 is rejected as unpatentable over Leamon U.S. 7323305 in view of Macevicz

(U.S. 6306597). Leamon has been discussed above. Macevicz is cited as teaching magnetic beads for attaching to polynucleotides. It is respectfully submitted that this rejection should be withdrawn for the same reasons as discussed for prior rejections: Leamon does not constitute effective prior art against the subject application. Withdrawal is respectfully requested.

A speedy allowance of all claims is respectfully requested.

Respectfully submitted,

Date: March 23, 2009

By: /Sarah A. Kagan /
Sarah A. Kagan
Registration No. 32,141

Banner & Witcoff, Ltd.
Customer No.: 22907